REMARKS

Claims 1, 6-8 and 11 are pending. Claims 2-5, 9-10 and 12-28 are canceled. Claim 1 has been amended. Support for the amendments to claim 1 can be found in the specification and claims as originally filed, for example, claim 1 as originally filed. No new matter has been added.

I. 35 U.S.C. § 112, first paragraph

Claims 1 and 4-11 are rejected under 35 U.S.C. §112, first paragraph. The Office Action at page 3 alleges that the specification, while being enabling measuring plasma concentration of ADMA in a pregnant woman at a stage of pregnancy from 23 to 25 weeks gestation, does not reasonably provide enablement for determining that a pregnant woman is at risk of developing pre-eclampsia by measuring ADMA at any stage of pregnancy or measuring ADMA levels in any tissue or body fluid of a pregnant woman.

Claim 1 has been amended to require measuring ADMA in a plasma sample taken from a pregnant woman at a stage of pregnancy from 4 to 25 weeks gestation, and determining that the woman is at risk of developing pre-eclampsia or her fetus is at risk of developing IUGR if the level of ADMA in the plasma sample is greater than 1.5 µmol/L. Thus, the claims no longer refer to any tissue or body fluid.

Regarding the Examiner's argument that measuring ADMA in a plasma sample taken from a pregnant woman at a stage of pregnancy from 4 to 25 weeks gestation would require undue experimentation, Applicants disagree. Undue experimentation would not be required to make and use the present invention over the range of 4 to 25 weeks gestation. MPEP §2164.08 states:

> The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'." *In re Wright,* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the

scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Applicants teach measuring asymmetric dimethylarginine (ADMA) in a plasma sample taken from a pregnant woman. One of ordinary skill in the art would know how to measure ADMA in a pregnant woman over the entire range of 4 to 25 weeks to determine the level of ADMA in the plasma sample. Likewise, one would know how to compare the ADMA level to the threshold level of greater than 1.5 μmol/L. Thus, one would know how to make and use the invention.

However, if one of ordinary skill in the art felt compelled to conduct their own study to validate the claimed invention, this could be done without undue experimentation:

> "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." *In re Colianni*, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). " 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing *In re Angstadt*, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976))...In the chemical arts, the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed. For example, if a very difficult and time consuming assay is needed to identify a compound within the scope of a claim, then this great quantity of experimentation should be considered in the overall analysis. Time and difficulty of experiments are not determinative if they are merely routine. [MPEP §2164.06]

As discussed above, one of ordinary skill in the art could measure ADMA levels and compare to the threshold level. Thus, one of ordinary skill in the art would be able to practice the claimed invention if desired. Applicants assert that the specification provides sufficient guidance to allow one of ordinary skill in the art to make and use the present invention without undue experimentation. Applicants respectfully request that this rejection be withdrawn.

II. 35 U.S.C. § 103

Claims 1-2, 4 and 5 are rejected under 35 U.S.C. §103 as obvious in view of Boger (WO 2002/14873) and Holden (Am J Obstet Gynecol. 1998; 178(3):551-6).

Claim 1 as amended requires a method of determining that a pregnant woman is at risk of developing pre-eclampsia or that her fetus is at risk of developing intrauterine growth restriction (IUGR). The method comprises measuring ADMA in a plasma sample taken from a pregnant woman at a stage of pregnancy from 4 to 25 weeks gestation, and determining that the woman is at risk of developing pre-eclampsia or her fetus is at risk of developing IUGR if the level of ADMA in the plasma sample is greater than 1.5μmol/L.

Boger describes methods and agents for detecting the probability of the future occurrence or progression of diseases that are associated with a disorder of nitric oxide (NO) metabolism. Holden describes a study of ADMA levels in women with pre-eclampsia and women without pre-eclampsia. Boger and Holden fail to disclose or suggest determining that a woman is at risk of developing pre-eclampsia or her fetus is at risk of developing IUGR if the level of ADMA in a plasma sample is greater than 1.5 μmol/L, as required by claim 1. Boger does not disclose measuring any level of ADMA in a pregnant woman. Holden does not disclose a level of ADMA in a pregnant woman of 1.5 μmol/L or greater. Therefore the combination of Boger and Holden does not render the present claims obvious. Applicants respectfully request the removal of this rejection.

In view of the above, applicant believes the pending application is in condition for allowance.

Applicant believes no fee is due with this response other than for the Extension of Time. However, if there are fees that are deficient, please charge our Deposit Account No. 06-2380,

under Order No. HO-P03236US0 from which the undersigned is authorized to draw.

Dated: May 21, 2009

Respectfully submitted,

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